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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/758,233	01/13/2004	Poul Egon Bertelsen	55682CON(71432)	5334

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EXAMINER	
SASAN, ARADHANA	
ART UNIT	PAPER NUMBER
1609	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/758,233	BERTELSEN ET AL.	
	Examiner	Art Unit	
	Aradhana Sasan	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *67-107* is/are pending in the application.

4a) Of the above claim(s) *97-107* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *67-96* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/17/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Receipt is acknowledged of applicant's response to Restriction Requirement filed on March 12, 2007.

Status of Application

Election/Restrictions

2. Applicant's election with traverse of Group I (claims 67-96) in the reply filed on March 12, 2007 is acknowledged. The traversal is on the ground(s) that since the present application is a continuation of USSN 09/786,864, which was the US national phase application of International Patent Application PCT/DK99/00480, the PCT rules concerning unity should be applied. This is not found persuasive because the instant application is not a 371 application, rather it is a continuation of a US national phase application, and US restriction practices can be applied instead of the lack of unity practice under PCT. Also, the search and examination of the three groups where species election was required (filler, alkaline substance, and preferred active substances) would involve searching a number of variants.

The election of species requirement is still deemed proper and is therefore made FINAL.

The election of hydroxypropylcellulose (HPC) as the filler, $NaHCO_3$ as the alkaline substance, and lornoxicam as the preferred active substance is acknowledged.

3. Claims 1-66 were cancelled (03/14/2005).

4. Claims 97-107 are withdrawn from consideration.

5. Claims 67-96 are being presented for examination.

Information Disclosure Statement

6. The information disclosure statement (IDS) submitted on 02/17/2004 was filed. The submission is in compliance with the provisions of 37 CFR 1.97 and 1.98. Accordingly, the examiner is considering the information disclosure statement. See attached copy of PTO-1449.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Regarding claims 78, 81, 82, 84, 89, the phrase "for example" ("e.g.") renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

9. Regarding claims 78, 81, 82, 84, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 67-96 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 8-17, 22-29, and 34-37 of U.S. Patent No. 6,713,089 ('089 hereafter). Although the conflicting claims are not identical, they are not patentably distinct from each other.

The claim limitations of each of the instant claims 67-96 would be obvious over '089.

Instant claims 67-70, and 75 would be obvious to a person with ordinary skill in the art over claim 1 of '089 which covers the claim limitations of: solubility of the active (at the most 0.1% w/v in 0.1N hydrochloric acid at room temperature), particle size of the active (at least 90% w/w of the active particles pass through a 180 μm sieve), pK_a of the active (at the most 5.5), particulate composition formed after powder contacting an aqueous medium, particle size of the particulate composition (at least 50% of the particles pass through a 180 μm sieve), release rate of the active (at least 50% w/w within the first 20 minutes) using the 0.07 N hydrochloric acid as the dissolution medium, and the composition comprising a pharmaceutically acceptable excipient. The difference between the instant claims and those of '089 is that '089 claim 1 discloses that when the dissolution of the pharmaceutical composition is tested, the active

substance "dissolves", as opposed to "releases" as in instant claim 67. A person having ordinary skill in the art would find that when a pharmaceutical composition is subjected to a particular dissolution test, and a certain percentage of the active ingredient "dissolves", it means that the active ingredient is "released" from the pharmaceutical composition into the dissolution medium.

Instant claim 71 (with the release rate limitation of at least 55% w/w of active within the first 20 minutes of the dissolution test) would be obvious to a person with ordinary skill in the art over claim 2 of '089. The difference between "dissolves" and "releases" is discussed above.

Instant claims 72, 73, and 74 (with the limitations of solubility of the active as at the most 0.05% w/v in 0.1N hydrochloric acid at room temperature, aqueous medium components water and organic solvent, and particle size of the particulate composition as 250 μm) would be obvious to a person with ordinary skill in the art over claims 3, 8, and 9 of '089.

The limitations of instant claims 76-96 (excipients, filler having binding properties, calcium hydrogen phosphate as filler, mean particle size of filler at the most 140 μm, alkaline substances, antacid-like substances, sodium hydrogen carbonate, mean particle size of antacid-like substance at the most 250 μm, NSAID (non-steroid anti-inflammatory drug) as an active substance, lornoxicam as an NSAID, further active drug substances (paracetamol etc.), dosage of active in the composition (1mg – 1.6g), dosage of lornoxicam in the composition (4, 3, 12, 16, 20, 24, 28, 32 or 36mg), water content of the composition at the most 5% w/w, and calcium hydrogen phosphate)

would be obvious to a person with ordinary skill in the art over claims 10-17, 22-29, and 34-37 of '089.

Since the instant application claims a quick release pharmaceutical composition and the claim limitations of the composition (active, alkaline substance, particle size, release rate, particulate composition, excipients), it is obvious over claims 1-3, 8-17, 22-29, and 34-37 of '089 and thus, they are not patentably distinct over each other.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 67-72, 74-78, and 81-95 rejected under 35 U.S.C. 103(a) as being unpatentable over Penkler et al. (US 5,854,226, '226 hereafter).

The claimed invention is a quick release (at least 50% w/w of the active within the first 20 minutes of a dissolution test) pharmaceutical composition for oral administration, comprising an active substance, such as the non-steroidal anti-inflammatory drug (NSAID) lornoxicam, that is poorly soluble (solubility of at the most 0.1% w/v in 0.1 N hydrochloric acid at room temperature), and is a weak acid (pK_a at the most 5.5). The composition is based on a powder (with a particle size where at least 90% of the particles of the powder pass through a 180 μm sieve), which contacts an

aqueous medium to form a particulate composition (with a particle size where at least 50% w/w of the particles pass through a 180 μm sieve).

Penkler et al. (US 5,854,226, '226 hereafter) teaches a pharmaceutical composition for oral administration comprising an inclusion complex of a non-steroidal anti-inflammatory drug (including lornoxicam), an alkaline earth metal bicarbonate, and further active ingredients.

The particle size claim limitation in instant claims 67-70, and 74 is obvious over '226. '226 teaches "pre-screened NSAID" (Col. 3, lines 65-66), and in example 4, teaches that the lornoxicam is screened (30 mesh) (Col. 5, lines 66-67). The 30-mesh screen is equivalent to a 600 μm sieve (according to the U. S. standard mesh sieve sizes provided by the ASTM), while instant claim 1 uses a 180 μm sieve (or an 80-mesh screen). A person having ordinary skill in the art at the time the invention was made would have found it obvious to use different particle sizes of the powder and the particulate composition in order to optimize the release profile. In order to enhance the quick release, a finer particle size (or a finer mesh screen) would be used to allow faster release of the active from the composition.

The instant specification discloses that the solubility of lornoxicam "is < 1 mg/100ml in 0.1 N HCl" (Page 6, lines 1-3) and "the pK_a value of lornoxicam is about 4.7" (Page 14, line 27). Since '226 uses lornoxicam as the active substance in the pharmaceutical composition (Col. 2, lines 31-34), a person having ordinary skill in the art would find the lornoxicam active in the instant application as an obvious component of the composition. Therefore, the solubility limitation of the active substance in instant

claims 67-68, and 72, and the pK_a limitation of the active substance in instant claims 69-70 would be obvious over '226 because the same active is used in the reference application.

'226 teaches the "gradual addition of deionised purified water" to the pre-screened NSAID mixture (Col. 4, lines 1-2). Therefore, the claim limitation of the powder being contacted with an aqueous medium of instant claims 67-70 is obvious over '226. Water as an aqueous medium would be obvious to one skilled in the art. The claim limitation of the particle size of the particulate composition (after the powder has been contacted with an aqueous medium), would have been obvious to one skilled in the art because the particle size of the powder prior to contact with an aqueous medium would be increased as a result of the "wetting process".

Regarding instant claims 67-70, the release rate limitation of would have been obvious to one skilled in the art over '226. '226 teaches a dissolution rate of lornoxicam as 80% dissolved within 30 minutes, using purified water (pH ~6.5, temperature 37°C) (Col. 6, lines 24-28, Fig. 2, Example 5). Instant claims 67-70 recite a "release" rate of 50% w/w of the active substance within the first 20 minutes at an acidic pH (0.07N hydrochloric acid) dissolution medium. A person skilled in the art would have found it obvious to test the dissolution/release of the active at various pH levels (especially acidic pH levels which are present in gastric conditions) during the process of routine optimization to ensure that the active will be absorbed by the circulatory system.

Regarding instant claim 71, the claim limitation of the 55% w/w release rate within the first 20 minutes would have been obvious to one skilled in the art given the

'226 teaching of dissolution rate. Also, during the process of routine optimization, a person skilled in the art would modify the formulation parameters in order to optimize the dissolution/release rate. See MPEP 2144.05.

Regarding instant claims 75-78, and 84, a person skilled in the art would find the excipient and filler having binding properties limitations obvious over '226 which teaches that the "pharmaceutical composition may also contain conventional excipients including binders ... diluents such as lactose, disintegrating agents, ... lubricants" (Col. 2, lines 50-54).

Regarding instant claims 81-83, and 95, a person skilled in the art would find the alkaline substance, sodium hydrogen carbonate (elected species), obvious over '226 which teaches "the alkali agent is preferably sodium hydrogen carbonate" (Col. 2, line 45). The mean particle size limitation of instant claim 83 would be an obvious variant to one skilled in the art during the process of routine optimization.

Regarding instant claims 85-87, a person skilled in the art would find the NSAID lornoxicam obvious over '226 which teaches lornoxicam in the pharmaceutical composition (Col. 2, lines 31-34, Col. 5, line 66, Example 4, Col. 6, lines 10-28, Example 5, and line 42, claim 1).

Regarding instant claims 88-90, a person skilled in the art would find the further active drug substance obvious over '226 which teaches a further active drug substance, including paracetamol (Col. 8, lines 9-12)

Regarding instant claims 91-93, a person skilled in the art would find the dosage of the active substance obvious over '226 which teaches unit compositions of

lornoxicam (Figure 2 with 4mg of lornoxicam). One skilled in the art would vary the dosage of the active ingredient, lornoxicam, in order to optimize the release/dissolution profile, and stability. The dosages recited in instant claims 91-93 would have been obvious variants absent any criticality or unexpected results.

Regarding instant claim 94, a person skilled in the art would find the water content limitation of at the most 5% w/w obvious over '226 which teaches a drying step after the addition of water and mixing (Col. 4, line 9). A person skilled in the art would reduce the water content of the composition in order to improve shelf life and minimize interactions and leaching, therefore, the water content limitation would have been an obvious variant found during routine optimization.

14. Claims 79-80, and 96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Penkler et al. (US 5,854,226), and further in view of Skinhøj et al. (US 6,599,529, '529 hereafter).

The teaching of '226 is stated above.

'226 does not specifically teach calcium hydrogen phosphate or hydroxypropylcellulose.

A person skilled in the art would find the calcium hydrogen phosphate and the elected species hydroxypropylcellulose (HPC) as the filler obvious over '226 in view of '529. '529 teaches calcium hydrogen phosphate and hydroxypropylcellulose as fillers (Col. 25, lines 8-22). The motivation to combine the references is provided by '529 which teaches that pharmaceutically accepted excipients are any materials which are

inert and do "not have any therapeutic and/or prophylactic effect" (Col. 24, lines 64-67). Therefore, the fillers listed in '529 would be obvious variants that a person skilled in the art would use in the process of routine optimization.

15. Claim 73 is rejected under 35 U.S.C. 103(a) as being unpatentable over Penkler et al. (US 5,854,226), and further in view of Penkler (WO 95/32737, '737 hereafter).

The teaching of '226 is stated above.

'226 does not specifically include an organic solvent as part of the aqueous medium.

A person skilled in the art would have found the limitation of the aqueous medium comprising water and an organic solvent obvious over '226, in view of '737. '737 teaches a pharmaceutical composition comprising a NSAID and a cyclodextrin and forming a paste with these ingredients and a "wetting solution". This wetting solution "may be selected from water, a lower alkanol, ... or a mixture of water and a lower alkanol" (Page 7). A person skilled in the art would be motivated to include a lower alkanol as an organic solvent along with water during the process of routine experimentation to make a particulate composition given the '737 teaching that a lower alkanol may be used in a wetting solution (or aqueous medium).

Conclusion

1. No claims are allowed.

2. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-

9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached at 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CECILIA TSANG
SUPERVISORY PATENT EXAMINER